

CLAIMS

1. A host cell transfected with a self-replicating polynucleotide comprising:
 - (a) a 5'-Non Translated Region;
 - (b) a HCV polynucleotide coding region encoding an HCV polyprotein comprising: NS3, NS4A, NS4B, NS5A, and NS5B proteins, said polynucleotide coding region comprising one or more amino acid substitutions selected from the group consisting of: R(1135)K, S(1148)G, S(1560)G, K(1691)R, L(1701)F, I(1984)V, T(1993)A, G(2042)C, G(2042)R, S(2404)P, L(2155)P, P(2166)L, and M(2992)T, and
 - (c) a 3'-Non Translated Region..
2. The host cell according to claim 1, wherein the host cell is a eukaryotic cell line.
3. The host cell according to claim 2, wherein said eukaryotic cell line is a hepatic cell line.
4. The host cell according to claim 3, wherein said hepatic cell line is Huh-7.
5. A RNA replication assay comprising the steps of:
 - (a) incubating the host cell according to claim 1 under conditions suitable for RNA replication;
 - (b) isolating the total cellular RNA from the cells; and
 - (c) analyzing the RNA so as to measure the amount of HCV RNA replicated.
6. The assay according to claim 5, wherein the analysis of RNA levels in step (c) is carried out by amplifying the RNA by real-time RT-PCR analysis using HCV specific primers so as to measure the amount of HCV RNA replicated.
7. The assay according to claim 5, wherein said polynucleotide encodes for a reporter gene, and the analysis of RNA levels in step (c) is carried out by assessing the level of reporter expressed.
8. A method for testing a compound for inhibiting HCV replication, including the steps of:

- (a) carrying step (a) according to claim 5, in the presence or absence of the compound;
- (b) isolating the total cellular RNA from the cells;
- (c) analyzing the RNA so as to measure the amount of HCV RNA replicated; and
- (d) comparing the levels of HCV RNA in cells in the absence and presence of the inhibitor,

wherein reduced RNA levels is indicative of the ability of the compound to inhibit replication.

9. The method according to claim 8, wherein said cell line is incubated with the test compound for about 3-4 days at a temperature of about 37°C.